REMARKS

Claims

Claims 19, 21–26 and 28–31 are under examination with claims 1–18 and 32–39 previously withdrawn from consideration due to restriction/election and claims 20 and 27 cancelled without prejudice or disclaimer.

Amendments

Support for the amendment of claim 25 can be found, at least, in the disclosure contained in the Examples. See, Example 2 and 3 and the description thereof in the paragraphs spanning pages 40–44 of the originally filed specification and the experimental data contained in Fig. 1. It is respectfully submitted that the amendments do not recite new matter nor do they narrow the scope of the claims. Entry thereof is respectfully requested.

Rejection under 35 U.S.C. §112, ¶2

Claims 25–26 and 28–31 stand rejected under §112, ¶2 as allegedly being indefinite. It is alleged that the claimed method is indefinite because the correlation between the level of B7H1 antibodies and the stage of the claimed disease/condition is not defined. Applicants respectfully disagree with this contention.

At the outset, it is submitted that the disclosure in Applicants' own specification, further in view of the references cited therein, provides a clear written description of the techniques that can be used in the assessment of disease stage of a pathological condition or disorder. To this end, the disclosure contained in, for example, Example 3 of the present application utilizes the art-recognized techniques for the assessment of the stage of a pathological condition or disorder based on observed clinical parameters. It is therein described that the *activity* of rheumatoid arthritis (RA) in a patient (i.e., a stage of RA disease in a patient) can be assessed by measuring tender joints, swollen joints, morning stiffness and/or elevated Westergren sedimentation rate and such *activity* correlated with the level of B7H1 autoantibodies in said patient. The Example and the data contained in Fig. 1H explicitly teach that "a significant correlation was found between *active* disease and the presence of hB7-H1-specific autoantibodies." Thus, the correlation permits distinguishing between active and inactive disease states. Recitation of *positive* or *negative* correlation, as required by the Examiner at page 4 of the Office Action, is not necessary at all. The same is true of the Examiner's contentions with respect to "higher level of antibody"

and "more advanced stage of disease." Withdrawal of the rejection is respectfully requested.

In light of the above considerations and amendments, Applicants request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

Rejection under 35 U.S.C. §112, ¶1

Claims 19, 21–26 and 28–31 stand rejected under §112, ¶1 as allegedly non-enabled. Applicants respectfully traverse this rejection.

To support the enablement rejection, the present Office Action raises two arguments:

(a) The Examiner acknowledges that the specification provides an enabling disclosure on the correlation between B7H1 antibodies and rheumatoid arthritis. He concedes that the disclosure in Fig. 1E and the description thereof in Example 2 of the specification explicitly teaches that the level of B7H1 autoantibodies is significantly elevated in RA patients compared to healthy volunteers ($p=0.0002$). However, he contends that this finding cannot be broadly used for diagnosing "other autoimmune disorders" because it would require undue experimentation. The Office Action then proceeds to allege that based on the decision rendered in *In re Wands* 8 USPQ 2d 1400(CAFC 1988), i.e., *Wands factors*, the scope of the claimed subject matter does not satisfy the statutory requirements under §112, ¶1. This contention is respectfully traversed.

Applicants aver that the PTO has failed to meet its burden of establishing that the disclosure does not enable one skilled in the art to make and use the antibody molecules in a manner recited in the claims. Instead of providing evidence of non-enablement, the Examiner cites the alleged lack of predictability in the art. The courts have placed a burden on the PTO to provide evidence shedding doubt on the disclosure that the invention can be made and used as stated. See example *In re Marzocchi*, 439 F.2d 220, 169 USPQ 367 (CCPA 1971). In contrast, the present Office Action has not presented any evidence to refute the findings described in Applicants' specification; nor has the Office Action established any scientific credibility to support the contention that the claimed disorders could not be diagnosed in a manner described herein. Therefore, the rejection under 35 U.S.C. §112 is improper.

Moreover, in view of the Remarks and the Exhibits filed with Applicants' reply of May 3,

2007, it is submitted that contrary to the Examiner's contentions, the autoimmune disorders claimed herein share a common property with respect to the levels of B7H1-specific antibodies. See, ¶2 at page 14 of Applicants' reply and the disclosure contained in the referenced publication by Dong et al. (*JCI*, 2003).

(b) The Examiner's allegation that the specification "does not provide sufficient enabling description of how to determine whether the level of recited autoantibodies in the sample is 'elevated.'" is misplaced. Firstly, explicit recitation of such is not necessary insofar as Applicants' specification and the reference publications cited therein provide art-accepted techniques for measuring the levels of such molecules in a biological sample of interest. Moreover, exemplary levels of such auto-antibody molecules in control specimens (for example, serum derived from healthy patients) are clearly provided in Examples 2 and 3 of the specification. Assays which are useful in measuring the levels of such antibodies, for example, ELISA assays are also clearly described. Based on this disclosure, the skilled worker has clear guidance on what baseline levels of B7H1 antibodies in "healthy volunteers" constitute. Using standard statistical techniques, one skilled in the art can reasonably ascertain what levels of B7H1 autoantibody molecules are clinically relevant for a particular condition. In case of RA, which is discussed herein as an exemplary clinical condition, the specification provides clear guidance that mean levels of B7H1 autoantibodies in healthy volunteers are about 0.5, while in RA patients, the value is about 1.0 (i.e., a two fold difference).

Applicants further submit that the metric used herein (i.e., optical density) is routinely used in quantification of protein concentrations and that the instant specification provides a detailed description of how measurement of such OD values can be utilized in the diagnosis of a disease and/or in staging procedure (for example, disease activity). See, e.g., the disclosure contained in Fig. 1E and Fig. 1H. In the case of rheumatoid arthritis (RA), the specification establishes that values above "cut off" OD450 (0.123) indicates positivity for RA in humans. Cut-off values for other disorders, for example, SLE, AHL, etc. can be determined using similar techniques. The level of experimentation would not be undue as such techniques (for example, ELISA assays) are routinely used in clinical investigation.

In view of the above remarks, it is respectfully submitted that Applicants' disclosure provides more than sufficient guidance to objectively enable one of ordinary skill in the art to

make and use the claimed invention with an effort that is routine within the art. The statute requires nothing more. Withdrawal of the rejection under 35 U.S.C. §112, ¶1 is respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,

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